

**From:** Jones, Samantha [Jones.Samantha@epa.gov]  
**Sent:** 8/27/2015 8:55:11 PM  
**To:** Newhouse, Kathleen [Newhouse.Kathleen@epa.gov]; Gibbons, Catherine [Gibbons.Catherine@epa.gov]  
**Subject:** RE: News Update: EPA Urges SAB To Clarify Concerns Over Novel Skin Cancer Risk Value (InsideEPA)

I know! Vince read this as we were wrapping up our Lean activities and all of a sudden he sorta gasped and said "This is me!"....He was wondering who the top risk assessor was and then realized they were talking about him! So ridiculous!

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**From:** Newhouse, Kathleen  
**Sent:** Thursday, August 27, 2015 4:30 PM  
**To:** Jones, Samantha; Gibbons, Catherine  
**Subject:** FW: News Update: EPA Urges SAB To Clarify Concerns Over Novel Skin Cancer Risk Value (InsideEPA)

Sometimes I wonder whether these reporters were at the same meeting I was! I feel like dermal issues were barely touched upon. Oh, by the way, if you didn't know, Vince is EPA's top risk assessor! So many weirdnesses in this article. Like shouldn't a science journalist know how to cite a scientific study? (I call this study Nesnow.) Good thing no one reads these articles!

## RISK POLICY REPORT - 08/25/2015

# EPA Urges SAB To Clarify Concerns Over Novel Skin Cancer Risk Value

Posted: August 24, 2015

EPA's top risk assessor is urging the agency's Science Advisory Board (SAB) to clarify its concerns that EPA should include additional studies to strengthen its novel skin cancer risk estimates in its draft risk assessment of the petroleum chemical benzo(a)pyrene (BaP), after the panel raised criticisms over most of the study's risk calculations.

The Chemical Assessment Advisory Committee (CAAC) panel, a subgroup of SAB, generally backs EPA's draft conclusions that the chemical is a developmental neurotoxicant, a reproductive toxicant, presents hazards to the human immune system and concurs with EPA's proposed classification of BaP as a human carcinogen.

But the panel's members have criticized EPA's approaches for calculating its first-time skin cancer risk estimate and its non-cancer inhalation and oral risk estimates, and questioned EPA's justification for its approach to its oral cancer potency estimate. The panel suggested that the agency should consider citing two additional scientific studies that it suggests might lend additional scientific support to a skin cancer estimate (*Risk Policy Report*, Aug. 4).

In response, EPA is countering that two studies floated by the panel would underestimate lifetime skin cancer risk from BaP because of their duration and is asking the panel to clarify those comments.

Vincent Cogliano, EPA's Integrated Risk Information System (IRIS) program director, noted in comments submitted ahead of an Aug. 21 CAAC teleconference that the agency sought to capture the studies "most appropriate" for analysis dose-response and deriving a cancer slope factor for lifetime dermal exposure, which is skin coming into contact with a substance. *Relevant documents are available on InsideEPA.com. (Doc. ID: 184200)*

Among the major criteria EPA used in the draft assessment, Cogliano wrote in the comments, was that a study should be approximately two years duration, or lifetime, and less-than-lifetime studies "would tend to underestimate lifetime risk by overlooking the potential for the development of tumors in later life."

Cogliano noted the studies suggested by the SAB panel -- a 1983 study, Nesnow, and a 1977 study, Levin -- treated mice for less than two years, and asks the panel to "elaborate on whether the relatively shorter durations of these two studies would decrease confidence in their utility for the derivation of a lifetime cancer slope factor?"

During the Aug. 21 CAAC teleconference, Cogliano said that those studies "wouldn't necessarily reflect a lifetime dermal estimate," adding, "I'd like the committee to reflect on that."

The draft BaP assessment is important for several reasons, including the first-time attempt to calculate a skin cancer risk estimate, something the agency has never included in another IRIS study.

EPA's effort at re-assessing BaP's risk comes at the recommendation of a 2010 SAB panel that peer-reviewed an agency effort at crafting a relative potency factor approach for estimating the toxicity of mixtures of polycyclic aromatic hydrocarbons, with the intent of using BaP as a reference chemical. That SAB panel pressed EPA to update its 1994 IRIS assessment of BaP before using it as a reference chemical in such an approach.

The draft assessment is also one of the first three being peer-reviewed by the relatively new CAAC, one of EPA's efforts to strengthen the IRIS program following a critical review from the National Academy of Sciences in 2011. The panel's comments to date have highlighted some concerns about the BaP findings.

**CAAC members used the majority of their time on the recent teleconference** to discuss the draft BaP review's dermal cancer slope factor (DSF). The panel's draft July 24 report says that EPA's proposed DSF for skin cancer is "not sufficiently supported scientifically," and urged the agency to consider the two additional studies and combining results from the mouse skin tumor bioassays in those studies to strengthen the value.

Epidemiologists on the CAAC panel previously raised concerns at the panel's meeting last April that EPA had not made sufficient use of studies of workers exposed to BaP on the job, particularly in the dermal and inhalation cancer potency estimates. They proposed that EPA consider epidemiology studies to bolster these risk estimates.

"The SAB also recommends that the EPA more thoroughly review the evidence of skin cancer in studies of coke, steel and iron, coal gasification and aluminum workers given their relevance for evaluating the appropriateness of using the mouse-based risk assessment model for predicting skin cancer risk in humans," the draft report says.

During the call, Miriam Poirier, of the National Institutes of Health, said that "historically there are more modern studies consistent with workers' risk of skin cancer," reiterating the calls for the agency to make better use of the worker studies, though she acknowledged the studies may have some sample size and other limitations.

The panel is raising also questions about EPA's proposed reference dose (RfD) for non-cancer adverse effects from ingestion, but for ingestion, raising questions over the basis for EPA's calculations, suggesting that a different effect might be more sensitive and a better endpoint on which to base the calculations. The RfD is the maximum amount that the agency estimates could be ingested daily for a lifetime without increased risk of adverse health effects.

For example, University of Washington's Elaine Faustman, who chairs the CAAC panel, noted on the call that EPA's RfD using neurobehavioral changes as an endpoint may "have the potential there for underestimating" because of limitations on the duration of exposure in the studies the agency relied upon.

The draft SAB report recommended that the agency "consider the overall picture of neurodevelopmental effects from a broader set of the neurodevelopmental endpoints to justify and support the choice of the critical endpoint."

Also on the RfD, some members questioned how EPA should include data on cervical hyperplasia, reiterating concerns that the agency should give more justification for not selecting an endpoint, but with at least one member saying "I'm not comfortable describing this as a reproductive effect."

Duke University's Edward Levin said that "there is always going to be some question of 'is it important'" when discussing a relatively new effect on tissue, but raised concern that such questions could delay EPA from setting a threshold limit for regulatory purposes. The panel also discussed its draft recommendation that EPA give greater consideration to genotoxic effects on male germ cells as a possible mode of action, noting that BaP is mutagenic because it can change genetic material and can therefore be detrimental to reproductive health.

"I'm not sure we want to go out on a limb and say there's not a genotoxic mechanism," Poirier said.

John DiGiovanni, of the University of Texas at Austin, noted that "I agree we wouldn't want to emphasize hyperplasia as a primary mechanism because there is evidence of mutagenesis as well." -- *Bridget DiCosmo*

Naseera H. Bland

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O: 703.347.0402

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